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LONG-TERM USE OF COLLAGEN HYDROLYSATE AS A NUTRITIONAL SUPPLEMENT IN ATHLETES WITH ACTIVITY-RELATED JOINT PAIN

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Purpose: Collagen hydrolysate is a nutritional supplement which has been shown to exert an anabolic effect on cartilage tissue. Its administration appears indicated in patients with osteoarthritis.
The purpose of the present study was to investigate the effect of collagen hydrolysate on individuals who are healthy and physically active.
Methods: A prospective, randomized, placebo-controlled, double-blind study was carried out at Penn State University in University Park (Pennsylvania). Parameters like joint pain, mobility and inflammation were evaluated with the use of a visual-analogue-scale during a 24-week-study-phase.
Between September 2005 and June 2006, 147 subjects who competed either on a varsity or a club sport were recruited. Data of 97 of those 147 subjects could be statistically evaluated.
Seventy-three subjects were randomly assigned to receive 10 grams of collagen hydrolysate per day in the form of a vial containing 25 ml of a liquid formulation and 74 subjects to receive a placebo, i.e. a 25 ml of a liquid formulation containing xanthan.
The primary efficacy parameter was the change of the visual analogue scales during the study phase in relation to the parameters referring to pain, mobility and inflammation.
Results: When the data of all the subjects (n = 97) that were evaluated during the study were taken into consideration, 6 parameters showed statistically significant changes of collagen hydrolysate (CH) versus placebo, namely the parameter “pain at rest” as assessed by the physician (CH versus placebo (-1,37 $\pm$ 1.78 versus -0.90 $\pm$ 1.74 (p = 0.025))) and the following 5 parameters as assessed by the study participants, “joint pain when walking” (-1.11 $\pm$ 1.98 versus -0.46 $\pm$ 1.63 (p = 0.007)), “joint pain when standing” (-0.97 $\pm$ 1.92 versus -0.43 $\pm$ 1.74 (p = 0.011)), “joint pain at rest” (-0.81 $\pm$ 1.77 versus -0.39 $\pm$ 1.56 (p = 0.039)), “joint pain when carrying objects” (-1.45 $\pm$ 2.11 versus -0.83 $\pm$ 1.71 (p = 0.014)) and “joint pain when lifting” (-1.79 $\pm$ 2.11 versus -1.26 $\pm$ 2.09 (p = 0.018)).
When a sub-group analysis which merely focused on subjects with knee arthralgia (n = 63) was carried out, the difference between the effect of collagen hydrolysate versus placebo even became more pronounced. It was the parameter “joint pain at rest” which was assessed by the physician with a p = 0.001 (-1.67 $\pm$ 1.89 versus -0.86 $\pm$ 1.77), plus the remaining five parameters which were based on the participants’ assessments like “joint pain when walking” with a p = 0.003 (-1.38 $\pm$ 2.12 versus -0.54 $\pm$ 1.65), “joint pain when standing” with a p = 0.015 (-1.17 $\pm$ 2.06 versus -0.50 $\pm$ 1.68), “joint pain at rest” with a p = 0.021 (-1.01 $\pm$1.92 versus -0.47 $\pm$ 1.63), “joint pain when running a straight line” with a p = 0.027 (-1.50 $\pm$ 1.97 versus -0.80 $\pm$ 1.66) and “joint pain when changing direction” with a p = 0.026 (-1.87 $\pm$ 2.18 versus -1.20 $\pm$ 2.10).
Conclusions: This is the first clinical trial to show improvement of joint-functioning in healthy subjects who were treated with the nutritional supplement collagen hydrolysate. The results of this study bear implications on the use of collagen hydrolysate as a primary-prevention-effort for individuals who are at risk of suffering from degenerative joint disease. Furthermore, the results also suggest that athletes consuming collagen hydrolysate can potentially improve their physical performance.

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A CLINICAL EVALUATION OF MATRIX-INDUCED AUTOLOGOUS CHONDROCYTE IMPLANTATION: FUNCTIONAL AND STRUCTURAL RESTORATION, AND PATIENT SATISFACTION

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Purpose: In comparison to conventional surgical treatment and periosteal autologous chondrocyte implantation (ACI), matrix-induced ACI (MACI) shows improved clinical outcome and technical simplicity. However, recent research suggests that the lack of measurement standardization across these studies, makes reliable large scale multi-centre cohort analysis extremely difficult. Hence, we have conducted both a prospective single-surgeon cohort study and a retrospective multi-centre satisfaction survey of over 200 MACI patients.
Methods: *Prospective Study:*
A consecutive series of 31 implantations were performed in 28 patients (18 male; 10 female) at a minimum of 24 months (mean age 36.5 years, mean BMI 25.9). Clinical assessment by the Six-Minute Walk Distance Test, and the self-administered Knee Injury and Osteoarthritis Outcome Score (KOOS) was conducted preoperatively, and at 3, 6, 12, and 24 postoperatively. MRI scans were conducted at 3, 12 and 24 months postoperatively. The relationship between MRI and functional outcome was also calculated. Graft failure was assessed postoperatively, both clinically and radiographically.
Retrospective Study:
Two hundred and two patients, 12 months or greater post-MACI, were surveryed. Patients with significant reoperation (realignment osteotomy etc) or cognitive impairment were excluded. The questionnaire was comprised of ten questions, based mainly on pain and symptom relief, functional restoration, quality of life, and patient satisfaction. Raw answers to the questionnaire were converted to a point scale to gain an overall satisfaction score (based on the Lysholm and Cincinnati scores). Clinical outcome was statistically compared to various cohort variables.
Results: *Prospective Study:*
Patients demonstrated a significant ($P<0.001$) improvement in six minute walk distance and all five KOOS subscales from 3 to 24 months after MACI surgery, with the most substantial gains noted in the first 12 months. Similarly, patients also demonstrated significantly ($P<0.001$) improved MRI scoring from 3 to 24 months, with post-hoc analysis again demonstrating improvement predominantly in the first 12 months, then plateauing thereafter. A moderate to strong relationship was observed between functional KOOS outcome and structural MRI outcome. A 10% incidence of hypertrophic growth following MACI was also observed.
Retrospective Study:
A mean age of the surveyed cohort was 36.9$\pm$10.7 (range 14-77) years, male:female sex ratio 114:88, and mean time from MACI to survey of 22.7$\pm$8.61 (range 12-49). Of note, 85% of patients rated their pain relief following MACI as good/excellent. 94% of patients stated they had the ability to participate in sport following MACI, 64% of patients reported no swelling after MACI, 81% of patents reported no occurrence of catching/locking, and 82% of patients rated the overall satisfaction of their MACI outcome as good or excellent. Statistical comparison between defined cohort variables and overall satisfaction score found significance between: postoperative months (12-24 months vs. over 24 months, P=0.03), rehabilitation participation (with rehab vs. without rehab, P=0.007), patient age (under 30 years-old vs. 30-50 years-old, P=0.001), and defect location (trochlea vs. patella, P=0.007; medial femoral condyle vs, patella, P=0.03).

Conclusions: The aforementioned clinical outcomes and comparative analysis is essential for furthering our understanding of the factors which influence patient outcomes in the treatment of cartilage injury by autologous chondrocyte implantation therapy such as MACI.

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EARLY REDUCTION IN ULCER COMPLICATIONS WITH LUMIRACOXIB COMPARED WITH NSAIDS: DATA FROM TARGET

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Purpose: A 79% reduction in upper gastrointestinal (GI) ulcer complications has been reported for lumiracoxib compared with nonsteroidal anti-inflammatory drugs (NSAIDs) (naproxen or ibuprofen) over 52 weeks in the non-aspirin population of the Therapeutic Arthritis Research and Gastrointestinal Event Trial (TARGET). However, guidelines indicate that these agents should be used for the shortest possible duration. We investigated how early after the start of treatment a significant benefit of lumiracoxib could be detected in TARGET.
Methods: TARGET randomized 18 325 patients >50 years of age with osteoarthritis (OA) to receive lumiracoxib 400 mg once daily (4x the recommended dose for OA) vs ibuprofen 800 mg three times daily or naproxen 500 mg twice daily for 52 weeks in one of two sub-studies. Randomization was stratified for age and low-dose aspirin use. The primary analysis population included patients not taking low-dose aspirin, comprising n=6950 patients treated with lumiracoxib and n=6968 with NSAIDs (naproxen, n=3537; ibuprofen, n=3431). The primary endpoint was the cumulative incidence of blindly and independently adjudicated definite or probable upper GI ulcer complications. The secondary endpoint was the incidence of definite or probable upper GI ulcer complications and symptomatic ulcers (all ulcers). In these analyses, pointwise 95% confidence intervals (CI) were generated for the between-treatment differences in Kaplan-Meier estimates (KMEs) for all ulcers and ulcer complications in the non-aspirin population.
Results: Based on the upper 95% CIs for the difference in Kaplan-Meier estimates, in the non-aspirin population there was a significant reduction in all ulcers by Day 8 with lumiracoxib compared with NSAIDs. For ulcer complications, a significant reduction with lumiracoxib compared with NSAIDs occurred by Day 16. When analyzed by sub-study, the advantage of lumiracoxib on all ulcers occurred as early as by Day 6 versus naproxen (Figure 1) and by Day 32 versus ibuprofen. For ulcer complications, a significant reduction was seen with lumiracoxib by Day 14 versus naproxen and Day 33 versus ibuprofen.

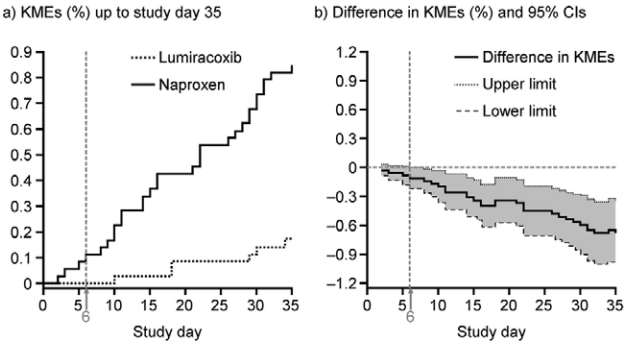

Figure 1

Conclusions: The long-term GI benefit of lumiracoxib compared with traditional NSAIDs has been demonstrated previously. However, even when given for short periods, the selective COX-2 inhibitor lumiracoxib appears to have significant GI safety advantages over nonselective NSAIDs.

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COMPARISON OF EFFICACY OF LUMIRACOXIB WITH CELECOXIB AND PLACEBO IN KNEE OSTEOARTHRITIS PATIENTS AND DIFFERING BASELINE DISEASE SEVERITY

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Purpose: To evaluate if the efficacy of lumiracoxib 100 mg od and celecoxib 200 mg od differed in patients with knee osteoarthritis (OA) as a function of baseline disease severity.
Methods: Data from two 13-week, multicenter, randomized, double-blind, double-dummy, placebo-controlled studies comparing lumiracoxib 100 mg od with celecoxib 200 mg od and placebo were combined for efficacy analysis based on baseline disease severity. The co-primary endpoints included assessment of OA pain intensity in the target knee (VAS), patient's global assessment of disease activity (VAS) and WOMAC™ LK3.1 total score at study end. Disease severity at baseline was defined as high, medium, or low using the median of the baseline values for each of the three primary assessments. A patient was classified with high baseline disease severity if all 3 baseline values were greater than their respective median, medium baseline disease severity if 1 or 2 baseline values were greater than their median and low baseline disease severity if none of the 3 baseline

Abstract 260 – Table 1. Efficacy of lumiracoxib in the disease severity subgroups at 13 week

Efficacy variable	Pair wise Comparison	High severity group		Medium severity group		Low severity group	
		Estimated difference (95% CI of difference)	P-value	Estimated difference (95% CI of difference)	P-value	Estimated difference (95% CI of difference)	P-value
OA pain	Lumiracoxib *vs* placebo	-9.30 (-13.25,-5.34)	<0.001	-5.48 (-8.41,-2.55)	<0.001	-4.74 (-8.44,-1.03)	0.012
	Celecoxib *vs* placebo	-6.70 (-11.22,-2.19)	0.004	-4.76 (-8.15,-1.38)	0.006	-4.74 (-9.03,-0.45)	0.030
	Lumiracoxib *vs* celecoxib	-2.59 (-6.44,1.25)	0.186	-0.71 (-3.67,2.24)	0.636	0.00 (-3.70,3.71)	0.998
Patient's global assessment of disease activity	Lumiracoxib *vs* placebo	-9.83 (-13.74,-5.93)	<0.001	-8.09 (-10.99,-5.20)	<0.001	-4.21 (-7.87,-0.55)	0.024
	Celecoxib *vs* placebo	-6.63 (-11.09,-2.18)	0.004	-6.10 (-9.45,-2.75)	<0.001	-3.47 (-7.72,0.77)	0.109
	Lumiracoxib *vs* celecoxib	-3.20 (-7.00,0.60)	0.099	-1.99 (-4.91,0.93)	0.181	-0.74 (-4.40,2.93)	0.694
WOMAC™ total score	Lumiracoxib *vs* placebo	-8.08 (-10.86,-5.30)	<0.001	-5.26 (-7.32, -3.19)	<0.001	-4.11 (-6.72,-1.50)	0.002
	Celecoxib *vs* placebo	-5.62 (-8.79,-2.44)	<0.001	-4.94 (-7.32,-2.56)	<0.001	-3.24 (-6.26,-0.22)	0.036
	Lumiracoxib *vs* celecoxib	-2.47 (-5.17,0.24)	0.074	-0.32 (-2.40,1.77)	0.767	-0.87 (-3.48,1.74)	0.513